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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,693	01/09/2002	Istvan Bakondi-Kovacs	2664/47002	5182
26646	7590	09/27/2006	EXAMINER	
KENYON & KENYON LLP ONE BROADWAY NEW YORK, NY 10004			MARX, IRENE	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/047,693	BAKONDI-KOVACS ET AL.	
	Examiner	Art Unit	
	Irene Marx	1651	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 August 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

Art Unit: 1651

### **DETAILED ACTION**

The amendment filed 8/22/06 is acknowledged. Claims 1-27 are being considered on the merits.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:  
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No basis or support is found in the present specification for the recitation "6"-O-carbamoyl tobramycin". Applicant's assertion in the response that applicants are allowed to be their own lexicographers is noted.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, definitions of chemical terms and/or formulae are not clearly encompassed by this proviso. There is nothing on the record to positively indicate that applicant had possession of the correct compound.

The bald allegation that "it is apparent to the person skilled in the art that only two functional groups, -NH<sub>2</sub> and -OH attached to the number 6 carbon atoms of two glycopyranosyl rings of the "6'-O-carbamoyl tobramycin" molecule can be derivatized" is not substantiated with appropriate evidence.

Upon presentation of appropriate evidence, the entire specification and claims should be amended to reflect the correct material intended.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1651

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-27 are rejected under 35 U.S.C. 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The written description and claims in the present specification are confusing and inconsistent in the recitation of the production of "6'-0-carbamoyl tobramycin". The compound intended appears to be "6"-0-carbamoyl tobramycin", as indicated in amended page 4, lines 22-24. However, the specification and claims have not been corrected at every instance, including at amended page 6, lines 14-18.

Consistent corrections at every occurrence are required. See, also the rejection under 35 U.S.C § 112, regarding new matter.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 lacks antecedent basis on claim 20 for feeding inorganic phosphate during the fermentation. Claim 20 pertains to adjustment of the pH of glucose solution prior to adding to the fermentation medium. Similarly, claim 23 is vague, indefinite and confusing in the recitation "per day". No antecedent basis is found for this recitation.

#### ***Response to Arguments***

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

In response to the allegations that the claim 20 should be "interpreted to mean that a glucose solution having a pH of between about 4.0 to about 5.0 is fed in step b) to regulate the constant level of the assimilable carbon source in the fermentation broth", it is noted that claim 20 is drawn to: "The process of claim 4, 5 or 6, wherein the constant level of the assimilable carbon source is regulated by feeding a glucose solution of a pH between about 4.0 to about 5.0".

Art Unit: 1651

First, there is no indication anywhere regarding the basis of "per day" in the process. Second, the timing of the pH adjustment is not set forth with any particularity in the invention as claimed. Third, there is no claim designated indication that pH-adjusted glucose is fed during the fermentation step b).

Therefore, the interpretation of applicants is not the only possible interpretation, which indicates ambiguity or lack of definiteness.

Therefore, the rejection is proper and it is maintained.

The rejection under 35 U.S.C 112, regarding deposit is withdrawn in view of applicant's averments.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Claims 1-4, 11, and 26-27 are/remain rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dinkov *et al.* (Bulgarian patent No. 50996), cited by applicant, but not proffered.

The claims are directed to a fermentation process for producing "6'-0-carbamoyl tobramycin" by regulating constant levels of assimilable carbon and nitrogen sources.

The reference teaches a fermentation process for producing 6"-0-carbamoyl tobramycin by regulating constant levels of assimilable carbon and nitrogen sources.

See, e.g., the claim and page 6, paragraph 1 of the Translation.

### ***Response to Arguments***

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant's argument that in Dinkov the addition is batchwise and that the levels of assimilable carbon source and assimilable nitrogen source are not maintained "constant", as required by the invention as claimed. The up and down swing of the concentration of assimilable carbon source and assimilable nitrogen source and theoretical calculations and varied assumptions have been duly noted. However, applicant fails to recognize that the claimed invention is not directed to a continuous process and that the "constant level" in claim 4, for example, has a range of about 0.001 to 0.5%. Therefore, no clear definition of the term "constant" as absolutely and totally devoid of up and down swings as alleged is to be found in this record. As a matter of fact, the term "constant" does not seem proper in the context of the claim designated invention. In

Art Unit: 1651

addition, only in claims 4-6 and 9-10 is a specific level of glucose as the assimilable carbon source indicated. In other claims some constant level that is constant at least at some time meets the claim. There is no claim designated requirement that the fermentation as a whole consists of steps a) and b). The use of the open language "comprising" does not limit the process to the steps specifically recited. Thus, the claim as written does not preclude the inclusion of further process steps in the process 6"-0-carbamoyl tobramycin, wherein the level of carbon is not "constant".

Although the argued elements of specific constant levels and specific carbon sources are found as examples or embodiments in the specification, they were not claimed explicitly. Nor were the words that are used in the claims defined in the specification to require these limitations. A reading of the specification provides no evidence to indicate that these limitations must be imported into the claims to give meaning to disputed terms.

Applicant's arguments that Dinkov maintains the concentration of glucose at 0.5% to 1.5% is noted. To the extent that the assimilable carbon source level is maintained at about 0.5% at any time, the invention as claimed is anticipated.

The arguments directed to the addition of sodium glutamate (Response, page 15, paragraph 2) are irrelevant to the invention as claimed, since nowhere is glutamate excluded as an assimilable carbon source.

Therefore the rejection is deemed proper and it is adhered to.

Applicant's arguments regarding claims 5-6, 9-11, 18 and 19 are persuasive.

Regarding claim 14, with all due respect, claim 14 is not included in the rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the

Art Unit: 1651

time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dinkov *et al.* taken with Ott *et al.* or Tomita *et al.* for the reasons as stated in the last Office action and the further reasons below.

Dinkov *et al.* teaches a fermentation process for producing 6"-0-carbamoyl tobramycin by regulating constant levels of assimilable carbon and nitrogen sources. See, e.g., the claim and page 6, paragraph 1 of the Translation.

The reference differs from the claimed invention in that the specific strains are not recited, in that glutamate is not specifically disclosed as a carbon source and in the use of inorganic salts such as ammonium salts and phosphate. However, each of Ott *et al.* or Tomita *et al.* discloses a fermentation process for the production of 6"-0-carbamoyl tobramycin. See, e.g., Examples. Ott *et al.* discloses a variety of suitable carbon and nitrogen sources, including amino acids such as glutamic acid (See, e.g., page 2, line 55 to page 3, line 13). In addition Tomita *et al.* discloses a similar listing of suitable carbon, nitrogen and inorganic salts such as phosphate. See, e.g., col. 11, lines 7-51.

The process conditions discussed in the references appear to be substantially the same as claimed. However, even if they are not, the adjustment of process conditions for optimization purposes identified as result-effective variables cited in the references would have been *prima facie* obvious to a person having ordinary skill in the art, since such adjustment is at the essence of biotechnical engineering.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of Dinkov *et al.* by feeding additional carbon sources, such as glutamate and using mineral salts such as phosphates as suggested by the teachings of Ott *et al.* and/or Tomita *et al.* for the expected benefit of maximizing the yield of the useful antimicrobial agent 6"-0-carbamoyl tobramycin.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

#### ***Response to Arguments***

Art Unit: 1651

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

In response to Applicant's argument that in the process of Dinkov the assimilable carbon source in the culture liquid moves up and down by at least 0.52% through the cycle of batch-wise feeding, it is of interest to note that the invention as claimed does not set forth a clear definition of "constant" in the claim designated invention. Only in claims 4-6 and 9-10 is a specific level of glucose as the assimilable carbon source indicated and in claim 4 the "constant level" fluctuates by "about 0.499%", which substantially includes "0.52%" when considering the upper limit provided by "about" and experimental error.. Therefore this argument fails to persuade.

The claims of record do not require a continuous feeding as the arguments appear to suggest by the emphasis on "batchwise" in Dinkov. It is submitted that both Dinkov and the invention are directed to substantially similar processes of "fed-batch".

Applicants argue that none of the secondary references relied upon by the Examiner teach or suggest the claimed process. However, "[n]on-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." In re Merck & Co. Inc, 800 F.2d 1091, 1097, 231 USPQ 375, 380 (Fed. Cir. 1986). The test of obviousness is "whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention." In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

The examiner relies on Dinkov for the disclosure of a fermentation process for producing 6"-0-carbamoyl tobramycin by regulating constant levels of assimilable carbon and nitrogen sources. The deficiencies argued by applicants in the secondary references fail to recognize that Dinkov is relied on for these teachings. The secondary references are relied on only for their disclosure of knowledge in the art of a variety of suitable carbon and nitrogen sources, including amino acids such as glutamic acid (See, e.g., Ott page 2, line 55 to page 3, line 13). As correctly noted by applicant, Dinkov does teach the addition of glutamate to the medium. In addition Tomita *et al.* discloses a similar listing of suitable carbon, nitrogen and inorganic salts such as phosphate. See, e.g., col. 11, lines 7-51.

Inasmuch as Dinkov clearly suggests that the maintaining of constant concentrations of an assimilable carbon source such as glucose and a nitrogen source such as ammonia nitrogen,



Art Unit: 1651

one of ordinary skill in the biotechnological arts would have recognized the desirability of further adjusting the process conditions for fermentation of *S. tenebrarius* for maximizing the production of the useful antibiotic 6"-0-carbamoyl tobramycin.

In addition, it is unclear that any data of record substantiates the contentions made in this regard using any microorganism, any assimilable carbon source, any assimilable nitrogen source and any level of "constant". Regarding applicant's arguments as to "unexpectedly much higher yields", the touted yields of Examples 4 and 5 are directed to specific strains of *S. tenebrarius* cultured under very specific process conditions.

The scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. In re Dill, 202 USPQ 805 (CCPA, 1979), In re Lindner 173 USPQ 356 (CCPA 1972), In re Hyson, 172 USPQ 399 (CCPA 1972), In re Boesch, 205 USPQ 215, (CCPA 1980), In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983), In re Clemens, 206 USPQ 289 (CCPA 1980). It should be clear that the probative value of the data is not commensurate in scope with the degree of protection sought by the claim.

Therefore these arguments fail to persuade.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

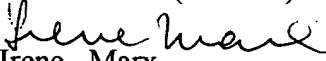
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1651

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Irene Marx

Primary Examiner

Art Unit 1651